



## Preface

# Clinical HIV-1 virology



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*Guest Editor*

It has been 8 years since the last issue on HIV-1 and AIDS was published in *Clinics in Laboratory Medicine*. Although it has been 8 years in time, it has been a quantum leap forward in both the basic and clinical science knowledge regarding HIV-1 infection. Over this time period, data on the viral life cycle and pathogenesis of disease states has increased remarkably. We now have a very good handle on viral replication on a molecular level in a variety of primary cell types, which is of importance in understanding AIDS pathogenesis. This interpreted into a revolution in antiretroviral therapy for HIV-1 infection. The development of combination chemotherapy (highly active antiretroviral therapy [HAART]) has led to a true paradigm shift in this disease. It is analogous to the change in diabetes care before and after the discovery of insulin. In the developed world, at least, much of HIV-1 infection has become a disease of chronicity. Many hospitals have remarkably fewer patients with HIV-1 infection admitted for care, and HIV-1 infection has become an outpatient disease in many cities in North America and Western Europe. This is based on the rational design of new drugs to inhibit HIV-1 in various portions of the viral life cycle, both preintegration and postintegration of the HIV-1 provirus. Unfortunately, these changes have not occurred in the developing world, which accounts for over 90% of the AIDS pandemic worldwide.

This issue of *Clinics in Laboratory Medicine* is extraordinarily timely and overdue. I have asked a variety of experts in critical fields in HIV-1 pathogenesis and clinical care to contribute important articles, which are designed to give a broad but clear overview of the developments in HIV-1 biology

and treatment over the past 8 years. The first article by Dr. Joseph DeSimone and myself demonstrates the new methods for detection of HIV-1, highlighting the increase in rapid and non-blood sample testing. The second article by Drs. Mark Holodniy and Karen Relucio discusses the importance of plasma HIV-1 RNA levels in understanding treatment effects and disease prognostication. This has been arguably one of the most important laboratory advances over the past eight years in HIV-1 clinical care. The next article by Dr. William O'Brien and colleagues takes on the Herculean task of reviewing the HIV-1 replication cycle. The amount of detailed understanding of HIV-1 replication and its interaction with host cell cofactors has been truly impressive over the last 8 years. As such, this is an important article for review by all physicians and scientists who approach HIV-1 either in the clinic or in the laboratory. Dr. George Hanna writes a very important and detailed review on HIV-1 genotype and phenotype resistance testing. Clearly, both secondary and the newly described primary resistance patterns found in HIV-1 viruses, caused by noneffective or semi-effective treatment, are two of the major problems that HIV-1 clinicians have had to face over the last several years.

I contributed the next article on HIV-1 reservoirs. This is a critical area in which HIV-1 latent proviruses, and cryptically replicating virus, in patients on virally suppressive HAART occurs throughout the epidemic. HIV-1 reservoirs are clearly the major reason that this lentivirus cannot be eradicated in patients on any known HAART regimen. The next article by Dr. Ron Collman and Dr. Linda Starr-Spires also is critical because it demonstrates the rational design of entry inhibitors, which are some of the newest therapeutic agents and which will likely obtain Food and Drug Administration approval in the next few years. Understanding the complexity of HIV-1 entry, which has had significant advances over the last few years, is key in the studies of therapeutic drug design.

Dr. Dennis Kolson contributes a section on HIV-1 neuropathogenesis. As the era of HAART has advanced, AIDS dementia complex has thankfully decreased in frequency. Nevertheless, this remains an enigmatic disease state in which neuronal drop out leads to a dementia complex, and is only now being understood on the molecular level. Immune reconstitution, in an article contributed by Drs. Drew Weissman and Luis Montaner, is also now of importance in the era of virally suppressive HAART. Many HIV-1-infected patients are left with a very low CD4+ T-lymphocyte count, even when the virus is decreased to undetectable levels in the peripheral blood. Clearly, immune reconstitution is of immense importance for long-term care in these patients. The next article, and arguably one of the hardest to synthesize based on its voluminous amount of material, is written by Dr. Ian Frank on antiretrovirals and HIV-1. With the explosion in antiretroviral agents over the last 8 years, this is a critical article for all physicians and scientists interested in HIV-1, who must be well-versed in this rapidly changing and expanding field. As a complementary article to the previous one,

Dr. Paul Palumbo describes both HIV-1 infection and treatment modalities in pediatric patients. Vertical transmission of HIV-1 is still present in the United States, although decreasing, and the pathogenesis and treatment of this disease in children is profoundly different from that in adults.

The next two articles are linked. The first by Dr. Charles Rinaldo and colleagues outlines the importance of CD8+ T lymphocytes and cytotoxic T lymphocytes in immunity against HIV-1 infection and inhibition of viral replication after infection. Clearly, for any immune-based therapy or vaccine design, understanding cytotoxic T lymphocytes and their interactions with HIV-1 is of critical importance. Dr. Matthias Schnell and colleagues write the final article in this issue, on HIV-1 vaccines. He and his group entitled this “The search continues.” I think that this is an appropriate title because we still, 21 years after the first AIDS cases were reported in the United States, are searching for an efficacious prophylactic or therapeutic vaccine.

I believe this issue is an extremely useful addition to the libraries of internists, infectious disease physicians, pathologists, and other medical scientists interested in HIV-1, and synthesizes the dramatic increase in knowledge regarding this pathogenic human retroviral infection obtained over the last 8 years. I look forward optimistically to the next several years, because I predict that there will be a continued dramatic increase in knowledge regarding the pathogenetic processes and treatment opportunities to combat HIV-1. It will certainly be interesting to see how the field changes over the next 8 years.

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